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SECTION OF BIOLOGY*

MARCH 10, 1947

DOCTOR R. L. MAYER, Research Laboratories, Ciba Pharmaceutical Products, Inc., Summit, N. J.: *Histamine and Antihistaminic Substances.*

Our paper on the anti-allergic properties of antihistaminic substances in reality covers three distinctly different fields, each of which is sufficiently important to justify separate discussion. It is impossible to deal with the action of antihistaminic substances without first discussing the object of their attack, namely, histamine; and it is not possible to discuss the use of these antihistaminic substances in allergic diseases without referring to the role that histamine plays in allergic diseases. Then, again, this talk would still be incomplete without mentioning those facts which prove that the so-called antihistaminic substances indeed counteract allergic manifestations because they neutralize histamine—*i.e.*, that there is a relationship between cause and effect.

We shall, therefore, become involved in a rather complicated triangle of three different problems which are not necessarily connected by short lines.

* The Section of Geology and Mineralogy held a meeting on March 3, 1947, at which Doctor M. L. Brashears, Jr., presented a paper on *Geologic and Ground Water Conditions on Long Island,* illustrated by lantern slides. No abstract of this has been received.

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Most of our synthetic drugs have been developed from time-honored, effective, but crude medicaments. The new powerful synthetic antimalarial compounds go back to quinine; the newer organic mercury compounds, used in syphilis, have their precursors in the mercury vapors of medieval mirror factories; while salvarsan was developed by Ehrlich, who knew that Fowler's solution had a beneficial effect in certain protozoal diseases. Other present-day useful remedies have been found by pure accident, such as the barbiturates and saccharine, to mention only two. However, today, there exist a large number of important synthetic drugs which are the result of pure theoretical speculation or systematic experimental research. The antihistaminic substances are a good example.

Pharmacodynamics of Histamine

As the name implies, the predominant property of antihistaminic substances is their ability to counteract histamine, that is, to nullify its toxic effects. The first question we shall attempt to answer is, therefore, "What are these actions of histamine which we want to counteract or nullify?"

Histamine is a regular constituent of the animal body and also a metabolite of certain bacteria and fungi. It is probably formed by enzymatic decarboxylation of histidine.

It is distributed throughout many organs with the white blood cells, the cells of the skin, the lungs, the liver, and the intestines being particularly rich in histamine. There are wide differences in its quantitative distribution. It seems more than fortuitous that the greatest amounts are found in the so-called border cells, that is, those cells which are in direct contact with the outer world. This may indicate that histamine plays a significant physiological role in the defense mechanism of the body against injuries coming from outside.

Dale and Laidlaw studied its pharmacologic effects in 1910 and found histamine to be a general stimulant of the secretion of various glands. It increases lacrimation and salivation and is one of the most potent stimulants of the gastric secretion. Furthermore, it strongly contracts the smooth muscles, especially those of the lungs, intestines, bladder, uterus, etc. The smooth muscle spasms produced by histamine are very intense: for example, histamine-induced spasm of the bronchial muscle of guinea pigs causes rapid death by suffocation.

In man and in certain animal species, histamine causes dilatation

of the capillaries and venules and, thus, hyperemia and skin wheals. In cats, dogs, and man, the blood pressure falls rapidly. Histamine apparently plays an important role as a mediator for certain sensations in the skin or mucosas, especially pain and itching.

Not all animals are equally sensitive to histamine. There are, in fact, great differences in susceptibility, which is a phenomenon rarely observed with other compounds. The most sensitive animals are guinea pigs, dogs, and man. For guinea pigs, an intravenous injection of doses as small as 0.3–0.5 mg. per kg. causes death. Dogs are killed by 1–3 mg. per kg. Man also is sensitive to milligram amounts. The mouse, rat, and frog, on the other hand, are very resistant to histamine, and toxic symptoms occur only after receiving doses of 500 mg. or more.

The ubiquitous presence of such a powerful poison in the animal body is quite surprising. No doubt, it would constitute a constant threat for the very life of the individual, were not the body equipped with certain mechanisms through which to check its toxicity. The most important protection is afforded by the fact that, normally, histamine does not exist as nor circulate in its free, active form; actually, it is bound within the cells, apparently to amino acids like arginine or lysine, to form an atoxic and inactive compound. Moreover, the body contains an enzyme, histaminase, first studied by McHenry and Best, which is able to destroy, by deamination, free histamine should it circulate in excessive amounts.

We do not know whether, under normal physiologic conditions, a steady liberation of free histamine takes place. Under the influence of certain pathologic stimuli, however, the sudden liberation of toxic amounts occurs. One of the most general of these conditions is a cell injury, such as occur during burns, injection of toxins and animal poisons such as snake or bee venoms, the presence of certain parasites like *Trichinella* or scabies, chemical or physical irritations of the skin, etc.

Rocha e Silva has speculated on the mechanism by which histamine is released from its inactive form. According to his theory, proteolytic enzymes, contained in certain toxins or activated by injury of the cells, split the polypeptide-like linkages. As soon as enough free histamine, now in its active and toxic form, enters the circulation, it will produce its specific toxic effects, provided that the animal species is sufficiently sensitive to histamine. This is an important point: Histamine is

liberated in the same proportions in either sensitive animals such as guinea pigs or in resistant animals like the mice. Toxic symptoms occur only in the former or sensitive group. In addition to the above-mentioned types of cell injury, one of the most important factors responsible for the liberation of histamine—important at least for the present discussion—is the combination of antigen and antibody as it occurs during anaphylactic shock and in certain other allergic manifestations.

The Histamine Theory of Anaphylaxis

Generally speaking, the combination of antigen and antibody and its direct consequence, cell injury, are the basis or cause for an outbreak of any anaphylactic shock. If we can prove that not only is histamine liberated during cell injury following an antigen-antibody reaction, but that it is also *responsible* for the manifestation of shock, then the first junction of the three pillars of the triangle, histamine-anaphylaxis-antihistaminics, has been made.

Shortly after the completion of their pharmacologic study of histamine, Dale and Laidlaw were struck by the strong resemblance between the symptoms of histamine poisoning and those of the anaphylactic shock. As is well known, anaphylaxis, which was thoroughly studied by Richet after the turn of the century and first described by him in 1905, is one of the most unusual phenomena in animal pathology. Anaphylaxis may be defined as a potential state of reactivity produced in certain animals by sensitization against otherwise harmless substances. In short, the general procedure for producing anaphylaxis is the following: A guinea pig or dog receives an injection of 1 to 2 cc. of horse serum, which does not produce any unusual effects. If, however, three weeks later, a small amount of the same serum is again injected, the animal responds immediately with an acute, often lethal reaction. In guinea pigs, for instance, the anaphylactic shock starts with itching, asthma, followed by general convulsions and death, all within a few minutes. It has been established that, during the three-week incubation period, specific antibodies against the sensitizing agent or antigen have developed. These antibodies are sessile, fixed to certain cells of the so-called shock organ, and combine, as already stated, with the reinjected antigen. This combination takes place in or on the very cells where the antibodies are fixed, and initiates the course of an anaphylactic reaction.

Almost from the very beginning, it was supposed that a toxic substance, an anaphylactic poison, is liberated during this cell injury. This poison was supposed to be the direct and final cause of the anaphylactic shock. It is to Dale and Laidlaw's great credit that they were the first to associate this anaphylactic poison with histamine.

Several observations have led to the identification of histamine as the direct cause of anaphylactic shock. There is, first, the striking similarity of many symptoms of histamine poisoning and anaphylaxis. Secondly, there exists a very definite relationship between sensitivity to histamine and the tendency to become anaphylactic: the more an animal is sensitive to histamine, the easier it becomes sensitized. Finally, there is much and varied experimental proof pointing to the liberation of histamine during anaphylactic shock.

For a long time, on the basis of these first two facts, the indictment of histamine as the principal offender was an indirect one. No suitable methods were available which would permit the detection of very small quantities of histamine (amounts in the order of $\frac{1}{10.000.000}$ of a gram per ml.) as they occur in the blood and other fluids. Systematic experimental studies on the histamine metabolism in anaphylaxis were only started almost 20 years after Dale and Laidlaw's publication, when Gaddum and his co-workers, Code, Rose, and others had devised suitable methods. Today, the evidence pointing to the release of histamine in anaphylactic shock in most animals is overwhelming, for Gaddum and Barsoum, Code, Rose, Dragstedt, and many others could detect significant increases of serum histamine during and immediately after anaphylactic shock.

The histamine theory of anaphylaxis has been extended, lately, to include many of the naturally occurring allergic diseases. Previously, anaphylaxis was considered as a pathologic entity of its own, and this term was restricted to experimental animals.

Today, we know that anaphylaxis is only a part of a more general pathologic process, namely, of allergy. Anaphylaxis is considered as a special form of allergy which not only can be experimentally produced in dogs or guinea pigs by sensitization with proteins, but which sometimes occurs in man.

Furthermore, certain food allergies or so-called constitutional reactions occurring in man after injections of medicaments or after allergic skin tests show some of the typical symptoms we encounter in experimental anaphylaxis. Most authors agree today with the con-

cept that anaphylaxis and the allergic diseases in man, such as food allergy, hay fever, pollen asthma, urticaria, and others are based upon the same mechanism. In all these cases, antibodies are formed which unite with the antigen, and in each instance it is the union of antigen and specific antibody followed by cell injury which produces the allergic symptoms. The principal difference between anaphylaxis and the various other forms of allergy is due to the location of cell injury and to the compositions of the injured cell.

We have much experimental data suggesting that histamine plays an important role in the symptomatology of many naturally occurring allergic diseases, as it does in experimental anaphylaxis. Increases in the histamine content of the blood have been found in cases of urticaria, hay fever, physical allergies, serum sickness, and others.

No doubt, the histamine theory offers a most appealing explanation for many phenomena occurring in anaphylaxis and other allergic manifestations. It satisfies our tendency for simplification. However, oversimplification distorts most facts. There are, indeed, many symptoms characteristic for anaphylactic shock, as well as many typically allergic manifestations, which cannot be explained by histamine release. Histamine, for instance, cannot be the cause for the loss of clotting ability of the blood during anaphylaxis in dogs. Furthermore, typical anaphylactic shock in rabbits, calves, and horses is not accomplished by a rise in the histamine content of the blood; in fact, there is a definite decrease. Certain authors therefore reject the histamine theory as a whole, or restrict it to certain symptoms. On the other hand, we must realize that the histamine theory does not necessarily postulate a rise in the histamine blood level.

Since it is known, today, that the antigen-antibody reaction takes place within the cells, we speak of the cellular theory of allergy, and no longer of the humoral. It is sufficient that histamine is liberated inside the cells, and it need not be released into the blood stream. However, it must be emphasized that the advocate of the histamine theory never intended to explain the entire process of allergy and all its symptoms only on the basis of histamine release. In addition to histamine, many other substances are liberated during cell injury, several of which are physiologically active, as, for instance, heparine, which is liberated after liver cell injury, various enzymes, glucose, etc., which in their turn may produce symptoms unlike those brought about by histamine. Histamine is only one, but nevertheless, in our opinion,

the most important factor in anaphylactic shock in certain animals and in certain forms of human allergy.

New proofs, pro or con, are needed in regard to the histamine theory. A new proof for the correctness of the histamine theory of anaphylaxis and certain other allergic symptoms would arise from experiments with chemical substances which specifically counteract or neutralize the pharmacologic and physiologic effects of histamine.

Antihistaminic Substances

Indeed, the following reasoning might have been made immediately upon the conception of the histamine theory of anaphylaxis. If the theory that the anaphylactic poison is identical with histamine is correct, then one would expect that a substance which nullifies the effect of histamine would also prevent anaphylaxis and all those symptoms of allergic diseases which are believed to be produced by a histamine release. Since experimental anaphylaxis and allergic diseases are so closely related, such an antihistamine substance would, therefore, not only confirm the histamine theory of allergy, but, at the same time, be the long-awaited remedy for hay fever, urticaria, and asthma.

However, this reasoning has only recently received its proper attention. In 1937, Bovet and Staub, of the Pasteur Institute of Paris, initiated a systematic search for substances capable of counteracting histamine. Among a great variety of compounds studied, they found two with high antihistaminic activity, namely, thymoxy-diethyl-ethylamine and diethylamino-ethylene-ethyl-aniline, the latter being three times more active. Both substances were able to nullify, in very small concentrations, the toxic effects of histamine on isolated guinea pig gut, lungs, etc., *in vitro*, as well as in the intact animal.

The French investigators then tried the two substances in anaphylaxis of guinea pigs and found that, in accordance with their prediction, both substances protected animals against shock. They concluded, from these results, that they had new and convincing proof supporting the histamine theory of anaphylaxis and, at the same time, an important contribution to anti-anaphylactic and, consequently, anti-allergic therapy. Unfortunately, both substances were so toxic for man that clinical use was impossible. These promising results led other workers to further their efforts to counteract histamine. They attempted to prevent anaphylaxis by the injection of histaminase, the

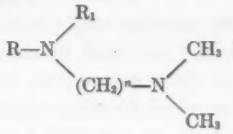
histamine-destroying enzyme which we have already mentioned. This method was definitely worthless in practice, although there was some effect in experimental shock. Equally unsuccessful were the numerous experiments and clinical trials made to counteract histamine by the process of desensitizing the body against histamine either by injections of histamine itself, or of histamine-protein complexes.

Bovet and Staub's investigations were interrupted when war swept over Europe. In 1941, the antihistaminic project was again taken up in France, and many compounds analogous to Staub's derivatives were prepared by Mosnier. His substances were tested by Halpern, who, in 1942, reported on two new derivatives of Staub's compound 1571F which were not only much more active, but, at the same time, considerably less toxic than the earlier products. One of these substances, Antergan, was introduced into the clinic with great success, which marked, after epinephrine, the first significant step in the chemotherapy of allergic diseases. However, this remedy produced, in spite of its increased activity and tolerance, an untoward number of unpleasant side effects and was, moreover, ineffective in many patients. Further modifications were, therefore, attempted which led to the preparation and introduction of new derivatives: Neoantergan in France, Antistine in Switzerland, and Pyribenzamine in this country. At the same time, Rieveschl and Loew prepared and examined substances which were modifications of the very first active compound which Bovet had described in 1937 as a strong anti-histaminic, namely, the thymoxy derivative 929F. Benadryl is a member of this group.

Let us return, for a moment, to our three discussion points. We have seen that histamine is a normal constituent of the body which is present in an inactive form; that, under certain conditions, histamine is set free, producing serious toxic symptoms. One of these conditions is the cell injury following the union of antigen and antibody. It is, therefore, theorized that histamine is responsible for the symptoms of anaphylactic shock and many other allergic manifestations.

Now, we learn that substances have been found which not only are capable of counteracting histamine, but which also protect against anaphylactic shock. There remains, in order to close our triangle, proof that these substances act as antianaphylactics and anti-allergics only or principally because they are antihistaminics. We shall, therefore, in the remaining portion of this paper, discuss the mode of action of these antihistamine substances and follow their various activities *in vitro* and *in vivo*.

Since the antihistaminic substances so far investigated all act in the same way, we shall discuss, here, the activities of one member of this group, Pyribenzamine. The general formula of substances of this kind is the following:



All substances found thus far to be among the most active substances conform to this formula.

Antihistaminic Activity

Antihistaminic activity *in vitro* has been tested by the usual methods, particularly by means of the guinea pig gut, guinea pig uterus, and isolated lungs and bronchi. Progressively more active compounds were found. Pyribenzamine shows an activity in concentrations as low as 0.02 per ml., while Halpern reports that a new substance, 3277 RP, a thiodiphenyl derivative, is, at least in this *in vitro* test, ten times more active. In the case of Pyribenzamine, it is evident that one molecule of Pyribenzamine neutralizes the action of 100 molecules of histamine. The antihistamine activity *in vivo*, when tested in guinea pigs, proves that there is a parallelism between the antihistaminic activity *in vitro* and that activity *in vivo*. Previous injection of 5 mg. of Pyribenzamine protects guinea pigs against 60 to 120 minimal lethal doses of histamine.

Anti-Allergic Activity

All these powerful antihistaminic substances protect guinea pigs from anaphylactic shock and, thus, become antianaphylactic remedies. If, with compounds within the same chemical group, we compare anti-anaphylactic activity with the antihistaminic activity, we find good parallelism. However, if we compare anti-anaphylactic and antihistaminic power of substances belonging to different groups, as, for instance, that of Pyribenzamine and Benadryl, the anti-anaphylactic activity is no longer directly proportional to the antihistaminic power. With Pyribenzamine, we obtain definite protection from anaphylactic shock in doses as small as 0.1 mg./kg.

Cutaneous Sensitizations

The clinical manifestations of allergy in man present the greatest variety of pictures, and there is no one organ which is not, in one allergy or another, affected in various ways and combinations. Until now, the allergic diseases experimentally reproduced in animals have been much less colorful, and restricted to certain types. Thus, it was possible regularly to produce in guinea pigs, by pretreatment with hog serum, generalized rashes which to some extent resemble general urticaria in food allergy in man, or generalized rashes in sensitizations to drugs. Pyribenzamine strongly counteracts this form of sensitization, thus proving that here, as in anaphylaxis, histamine plays a predominant role.

One of the most common allergic manifestations in man and in many animals is contact dermatitis, or eczema, and it is the general assumption that, contrary to urticaria, these diseases are based upon a special mechanism different from that responsible for urticaria or hay fever. It is likely that, here, substances other than histamine are involved. Indeed, Pyribenzamine and the other antihistaminic substances are least effective in these forms of allergies in man. However, in experimental sensitizations of dermatitic type, which we produced in guinea pigs by pretreating them with paraphenylenediamine, Pyribenzamine was quite active, although the doses required were very high. The effectiveness of Pyribenzamine was especially noticeable when Pyribenzamine ointment was locally applied. It seems that Pyribenzamine ointment is also effective in many cases of itching dermatoses in man.

Having seen, now, that these substances neutralize the activities of histamine *in vitro* and *in vivo*, there remains the question of explaining the mechanism of action. Histamine may be neutralized in different ways: The first method would be to prevent the formation of free histamine; or it should be possible to destroy it, as has been attempted by the introduction of histaminase; or, finally, there should be a means of preventing it from producing its physiological and pharmacological activities. This latter method is precisely what antihistaminic substances accomplish. It has been experimentally proved that they do not prevent the release of histamine, nor do they destroy released histamine. On the other hand, they do prevent histamine from exercising its typical activities. They supposedly prevent hist-

amine from reaching those cells or enzymes to which histamine normally becomes anchored, and they are capable of occupying those places which histamine normally would occupy. In other words, antihistaminic substances compete with histamine for the normal histamine-receptive sites.

For this reason, no histamine effects appear. The same mechanism of action has been proposed for the neutralization of sulfonamides by PABA. And as PABA and sulfonamides are chemically related, so is there also a certain similarity between antihistaminic substances and histamine.

Since these antihistaminic substances do not influence the liberation of histamine but act only upon the last phase of the anaphylactic chain reaction, they do not constitute any etiologic therapy, but afford only symptomatic relief. Etiologic therapy would consist in using substances which prevent either the production of antibodies, the union of antigen and antibody, or the release of histamine from this union.

We have not discussed, here, the toxicity of the different antihistaminic compounds or the side effects occurring during their therapeutic use. Unfortunately, these are quite numerous. Therefore, throughout this country, intensive research has been started for the development of new products which will produce less side effects, and it is quite probable that our present substances will serve only as the important starting-point for a series of more effective remedies for allergic diseases.

In closing this discussion, I trust that I have been able to create interest in the complicated but very fascinating problems which arise when we speak of antihistaminic and anti-allergic substances.

SECTION OF PSYCHOLOGY

MARCH 17, 1947

DOCTOR KURT GOLDSTEIN, Visiting Professor of Psychology, College of the City of New York, New York, N. Y.: *Organismic Approach to the Problem of Motivation.*

"The problem of motivation," writes Boring, "is the problem of determining the forces which impel or incite all living organisms' actions."

It is not and cannot be my intention to take into reference the enormous research undertaken in this field, to discuss the different attempts to solve the problem, and to deal with it in all its implications. What I intend to do is to draw attention to some observations which seem to me suited to contribute something to our knowledge of these forces, and which support an organismic approach to the problem of motivation.

In all the cases I wish to refer to, we are facing the process of adjustment to an irreparable functional defect due to a damage of the brain. The way in which this adjustment is achieved gives us some insight into the motives of organismic behavior. These patients who show a number of defects—differing as to the location of the damage—must find adjustment to their functional defects. Otherwise, they are in danger of deteriorating increasingly. They are, thus, under the urge of a strong force like the normal organism if its activity is determined by a strong 'drive.'

The condition of such a patient during the first time after the incident occurred—it may be an injury, a hemorrhage, or any other disease which produces a more or less circumscribed damage to the brain—is best characterized as a state of *general disorder*. The patient is not only incapable of performing tasks he could perform before; he is, besides that, changed in his total behavior, he is restless, distracted, inconsistent, frightened, very emotional; he cannot fulfill tasks in which he is apparently not damaged. He is in a state which I have called 'catastrophic condition.'[1] After a certain time, his behavior changes. He shows greater constancy, is more quiet, no longer seems

[1] See, **Goldstein, K.** The Organism. A Holistic Approach to Biology: 35 ff. American Book Company. New York. 1939.

so often stricken by anxiety. The organism seems to have reached again a state of order, of equilibrium. What is the cause of the condition of disorder, and which are the forces that bring about the new order?

To answer these questions, we have to look at how the order and constancy of the normal organism are guaranteed. The basis of order is the constancy of the thresholds of the organism. If the thresholds would not remain approximately equal under 'normal' conditions (in the outer world and inside of the organism), a stimulus corresponding to an object or an event would not arouse about the same effect and the same experience, nor would the organism be able to react to the same situation in a consistent way. Our world would change incessantly, and we ourselves would change, too. Our personal existence would always be in danger. As a matter of fact, however, this is not the case. Our world remains relatively constant, despite all the changes in it, and so do we ourselves.

On the other hand, there is no doubt that each stimulation produces a change in the psycho-physical substrata by which its excitability is modified, with the result that a new stimulus, equal to the former one, gives rise to an effect different from the previous one—or, better said, would give, if there were not a mechanism at work by which that is prevented, by which the threshold is brought back to its previous, normal height after a definite period of time. This mechanism, which we call the *equalization process*,[2] is a basic biological phenomenon. It keeps the thresholds constant and is also the presupposition of ordered behavior, which guarantees the existence of the organism. This normal equalization process, in any part of the organism, is dependent upon the normal functioning of the total organism, as I was able to show on another occasion.[3] If a part of the organism is separated, 'isolated' from the rest, the equalization process is modified in this part. Stimulation here produces abnormal reactions, and ordered behavior is more or less impossible. This happens in pathology. The organism is no longer able to come to terms with the demands of his previous milieu. Disordered reactions, catastrophes, and anxiety are the consequences. That is the condition in which the patient is in the beginning.

[2] Ibid.: 113 ff.
[3] Ibid.: 111.

How does he return to the state of order, if his impaired capacities do not come to the norm? As a matter of fact, he has the same defects in the state of order, but they no longer come to the fore in a disturbing way. That, however, is not the whole picture. If we compare the results of examination of the different performance capacities with the behavior of the patient in everyday life, we find an astounding discrepancy. Such comparison reveals, on the one hand, that the patient performs better in the latter condition (as we shall see by finding compensations for his defect); and, on the other hand, that he does not at all utilize all the possibilities of the preserved capacities. He seems to stick to some definite performances. This rigidity of behavior is usually attributed to a special anomaly called perservation. Closer investigation shows that there is no evidence to assume such a general anomaly; that the patient is not at all perseverating under all conditions; that he sticks to such performances as he can fulfill, and only if he is confronted with a task he cannot fulfill[4] does the perseveration occur. If examination is organized in a way that tasks of a kind which the patient cannot fulfill are avoided to a certain degree, he does not perseverate or only much less. Why does he perseverate if he is confronted with insoluble tasks? Because the insolubility of the task may produce a catastrophic condition, and with that make it impossible for the patient to use even his preserved capacities. Catastrophic condition does not only eliminate performance momentarily but has a disastrous effect on the activities following for a certain shorter or longer time. Thus, 'self-realization' of the organism and its 'existence' are in danger. That is what the organism tries to avoid by sticking to the performances it is able to fulfill, if confronted with such tasks as it cannot cope with. This prevents occurrence of catastrophic condition.

Now, the patient (as long as he is living in his old milieu) is easily and frequently confronted with tasks he cannot solve and, so, exposed to the entrance of catastrophe. This goes along with the experience of abnormal tension. It is only too natural that the sick organism tends to remove this dangerous condition by all means. Only then will it remain at least in a certain order. Thus, it seems to be governed by a 'drive' to eliminate tension, *to find release of tension*, which is at least temporarily achieved by sticking to a task it can master.

[4] **Goldstein, K.** Physiological aspects of convalescence and rehabilitation, etc. Symp. Physiol. Aspects Convalescence etc., Fed. Proc. Exp. Biol. 3: 260. 1944.

All I have said about the behavior of organic patients is valid also for so-called neurotics. On the onset of the development of neurosis, disorder and anxiety stand in the center, as expressions of the impossibility to come to terms with tasks set for the individual, and of the experience of not being able to realize his or her own personality. This anxiety may be due to conflicts in infancy or later life. I cannot discuss this complex problem here. Such a discussion would bring us too far away from our subject and is not essential for the problem we are interested in. We are interested in the motives which bring about the elimination of disorder and anxiety in neurotics. The neurotic organism tries as well as the organic to get rid of disorder, by the same reason and by the same means. This it accomplishes by building up protective mechanisms which consist mainly in sticking to such performances which it can fulfill (in spite of the conflicts) and which prevent the conflicts from coming to the fore and, with that, unbearable tension. The result is the well-known compulsive behavior, which is not simply an expression of disease but mainly a protection against the danger of tension and of catastrophes. The significance of compulsive behavior shows up when one tries to force the patient to give up his compulsive actions. Then he comes into a state of enormous tension, anxiety, confusion, aggressiveness, *i.e.*, catastrophe. If he is allowed to stick to his compulsions, the patient is able to fulfill so many tasks that he can realize his personality at least to such a degree that life to him appears worth living. He appears forced to follow definite drives, trends, desires, and does so for the sake of getting rid of tension. His whole behavior seems to be dominated, motivated by getting release of tension, like that of the organic patient.

From such observations, one might be induced to consider the trend to come into a state of equilibrium, into order—the trend for release of tension—a basic motivating force of organismic life. This corresponds to a theory of motivation which has obtained widely spread appreciation. This theory considers the important, if not the essential motive of behavior elimination of tension, which appears as an expression of the various drives which are supposed to motivate organismic life. The goal of the drives, according to this theory, is the elimination of the disturbing tension which they produce. The best known expression of this tension-release theory is the pleasure principle of Freud.

I think we are not justified to make such a conclusion from the observation of patients, and that for the following reasons:

The domination of behavior by the tendency to release tension is a *pathological* phenomenon. It is an expression of defective functioning of the organism. As I was able to show in many examples, it is the effect of stimulation of parts of the organism isolated from the total organism. It is the effect of isolation, and the most characteristic consequence of pathology. The pathological organism is forced into these reactions, but they are not its goal. The real motive of the activities of the pathological organism is, like that of the normal, the trend to realize its capacities. It tries to realize the preserved capacities in the best possible way. The behavior of patients with brain damage, as that of neurotics, can be understood only from this point of view. It is a basic mistake of the tension-release theory of motivation that it tries to interpret normal phenomena from laws determining abnormal life *without taking into consideration the phenomenon of pathology*. This brings the theory to overlook that the trend for release of tension is in the foreground to such a degree because, for these individuals, it is the absolute presupposition for ordered behavior and, with that, for self-realization at least to a certain degree. Indeed, the tension-release theory is not based on pathological material alone, but also on observation of young children and animals under experimental conditions. The phenomena observed here are, however, also modified by the influence of isolation, which is here effective in a way similar to that in pathology. We have no time, here, to consider the effect of the 'fallacy of isolation' and its theoretical and practical implications. I wish to point to my discussion of this very important problem on another occasion and stress only a few points. The theory which considers a drive for maintenance or self-preservation as the basic drive of organismic life is due to the above-mentioned fallacy. Preservation is an expression of pathology, of decay.[5] The goal of the normal organism is not preservation of an existent state. The tendency of normal life is directed toward activity and progress.

The facts which seem to speak for the *existence of special drives* do not correspond to the natural behavior of the organism. They are *special reactions*, in special situations, of the total organism under

[5] See, **Goldstein, K.** Human Nature in the Light of Psychopathology: 147. Harvard Un. Press. 1940; also, The Organism: 443.

special unusual conditions. If the tension corresponding to a special deficiency of the organism, *e.g.*, of nutrition or sex, etc., increases to a certain amount—because of abnormal conditions in the outerworld or within the organism—then the organism may be disturbed in general, in a way that catastrophe and, with that, impossibility to realize its nature are impending. Then, the deficiency must be eliminated by all means, and, under these circumstances, the organism appears motivated in its behavior by hunger, thirst, sex, etc. Under normal conditions, we are not forced to follow such needs even if they are strong. If we are involved in a very important activity, the neglect of which would bring us into danger, then we do not follow such needs. We give way to them if this is not in contrast to the activities of self-realization, or if it belongs to these. The impression of special drives appears when we consider the activities of the organism isolated from their relation to the total organism.

This and similar assumptions are due to the neglect of the fact that definite reactions belong into a special context and cannot be transmitted to others—the *neglect of context*, as John Dewey has termed this phenomenon, which he, in an interesting paper about context and thoughts, calls "the greatest disaster which philosophical thinking can incur." By this neglect, through the fallacy of isolation, elements belonging to a special context become absolute by the fallacy of *universalization* and are often "converted into sweeping metaphysical doctrines." Indeed, consideration of the belonging of special phenomena to a definite context is not sufficient for understanding organismic behavior. It will prevent us from making too quick generalizations of observations made under certain conditions. But it does not render possible a decision as to whether a phenomenon belongs to the 'context' of the organism. For such a decision, the concept of 'self-realization' seems to present a possibility.

The traditional view assumes several drives which become effective according to the intensity of the individual drive. That is true. The intensity can, however, be evaluated only in relation to the total organism, by its value for the latter's self-realization under the given conditions.

Our standpoint has another valuable consequence. We are able to understand, from here, the *positive significance of tensions*. The organism is not only driven sometimes by the tendency to release tension, but it accepts tension *as a positive experience*. Normal behavior

corresponds to a continual change of tension of such a kind that, over and again, that tension is reached which enables and impels the organism to further activities according to its nature.[6]

The *tension-release theory* (as, *e.g.*, in the form of Freud's) knows only the *urge to release*, not the *pleasure of tension*, which is not only at the basis of all creative activity, but also an essential part of the pleasure corresponding to all so-called lower needs, as hunger, sex, etc.

Certainly, I do not want to deny that there are also normal conditions in which the need for rest and release of tension is in the foreground. Also, normal life is full of catastrophes, and we can fulfill our goals only if we have intercessions of rest and release of tension. But how much we submit to these needs, is determined by their significance for self-realization of the total organism. If they come to the fore as *all-determining* forces, then there is something wrong with the total organism, with the personality.

It may seem that I have drawn on the pathological observations mainly from the standpoint of warning against too simple an application, to the interpretation of normal behavior, of the laws found valid there. However, I also stressed a positive factor as a motivating force which, admittedly, did not come to the fore so much in the first part of this paper, though it already showed its great significance, *viz.*, the trend of the sick organism to utilize its preserved capacities as much as possible. To stress this factor is the purpose of my further discussions, which will use the procedure in adjustment to a circumscribed irreparable defect as a basis for determining the motivating force.

Because the organism must be very careful concerning the occurrence of catastrophes, it has to restrict itself in the utilization of all its preserved performances: a selection has to take place. This selection becomes understandable if one considers it from the angle of inquiring by which performances the goal, self-realization, can best be reached and catastrophes may be avoided at the same time.

I should like to illustrate this assertion by two examples, the behavior of patients with hemianopsia and with disturbances of equilibrium due to cerebellar lesions.[7] Hemianopsia is total blindness of corresponding halves of the visual field in both eyes due to lesion of

[6] The Organism: 197.

[7] As to the facts, see, **Goldstein, K.** The two ways of adjustment of the organism to cerebral defects. J. Mount Sinai Hosp. 9(4): 504. 1942; also, The Organism: 47 ff.

the occipital lobe of the brain. Behavior of these patients in everyday life often fails to indicate that they do not see in one half of the field. They are subjectively aware of a somewhat impaired vision, but they see objects in their entirety, not only halves of them. Their visual field is arranged around a center like in normal people, the region of clearest vision lying *within* this field—not, as one could assume, on the margin corresponding to the location of the fovea in the preserved half of the field. I cannot explain, in detail, how the organism manages to obtain a whole field. I wish to stress the fact that research has shown that only if the object one wants to see is within a field good vision and recognition are guaranteed. This has to be reached by the patient, and it is achieved by a little deviation of the eyes, so that the visual stimuli coming from all sides are then reflected on the healthy retina. This is the only way to enable the individual to have visual performances which make recognition of objects possible, and it apparently occurs. Only from this point of view the new organization becomes intelligible. It is apparently *the goal of the organism* to have a vision as good as possible, and that was the motive of the activity.

This assumption is confirmed by another observation. The transformation mentioned does not take place if the one half of the visual field is not *totally* lacking perception, as in cases of hemiamblyopia, where vision in the one half is diminished but not so much that it could not be used for essential performances and, particularly, for rendering possible the normal, characteristically formed, visual field.

As long as such is the case, transformation does not occur, and it does not do so because it is not necessary, since the diminution in vision in hemiamblyopia is not so disturbing that recognition of objects cannot take place. This state has some advantage over that of transformation. The latter limits other performances of the organism. After transformation, the field is constricted, and by displacement of the eyes the total organism is restricted in some performances. The organism bears all these impediments if a good vision—a performance so essential for the total organism—cannot otherwise be reached, as in total blindness of the halves of the visual field. It avoids them if adequate vision can be maintained to some degree, sufficient for the most important performances for the total organism: *recognition of objects*, without eye-shifting with its consequences. Apparently, what is pertinent is not the best possible performance in *one* special per-

formance-field but the best possible activity of the organism as a whole. Here lies the motivation for the particular form of adaptation, the cause of the differences of adaptation in hemianopsia and hemiamblyopia.

Another example from a totally different field will illustrate the same procedure of the organism in adjustment to a circumscribed defect.

In some patients with cerebellar lesion, one observes tilting of the body and the head toward the side of the lesion—in left-sided lesions to the left side. In other cases, however, with a similar lesion, the head is tilted to the other, the right side.

What is the cause of the deviation and of the difference in some patients with the same lesion of the cerebellum?

Closer investigation shows that the patient can stand and behave quite normally in all other performances, bodily and mentally, if he has head and body a little tilted to the left side. If he is forced to bring his head into the previous normal, erect position, he is not only in danger of falling to this side, but he feels dizzy, confused, and cannot fulfill other physical and mental performances in a normal way. He feels well and returns to the norm in all these respects if he is allowed to keep his head tilted sideways.

If he keeps his head straight, he experiences a pull to the affected side. This pull corresponds to a normal tendency of the organism *to turn toward stimulation* from the outside, stimulation of the skin, ear, eye, etc. The organism is thrown to the side of stimulation. The normal individual does not feel this pull because both sides of the body are normally stimulated in about the same strength and, so, the pulls to both sides counterbalance each other. Thus, an equilibrium is established which is further guaranteed by the regulative influence of the cerebellum and frontal lobes, and we stand up straight without difficulty. In the patient, the reaction is abnormally strong on one side because of the lesion of the cerebellum of the corresponding side. The organism is thus thrown to this side by the stimuli originating from the normal outerworld. If the patient tilts his head, the pull disappears. The abnormal position represents an adjustment of the organism to the defect, and brings about a new order. The organism is able effectively to utilize its capacities to a higher degree because of the lack of catastrophes. The patient finds by, so to say, yielding to the abnormality, to the abnormal pull, a better, more constant condition.

The deviation becomes so understandable from the motive that the organism tries to get a condition in which it is in a *situation to realize its capacities best.*

Now, why does the other type of patient, suffering from the same defect, hold the head *tilted to the opposite side?*

If one examines these patients carefully, one finds that they have the same defect, but in a *different degree.* The pull has the *same direction* but is *much stronger.* In the first group of cases, the patient shows a *tendency* to fall if he keeps his head upright, in the second the patient *falls really,* his stability thus being affected to a much higher degree, and he is more easily thrown into great disorder with disturbance of all performances. If this patient followed, in his attempt to adjust to the defect, the same course as the first one, *i.e.,* if he yielded to the pull, he would have to assume an extreme position in his attempt to compensate the stronger pull by tilting the body. By this position of the whole body, no balance could be maintained at all. Such an attempt of adjustment to the defect would not bring order, and, thus, the behavior of the organism as a whole would not be guaranteed. Therefore, another way of adjustment has to take place, namely, the pull to the left side is compensated by the production of a voluntary pull to the other, the right side. This is achieved by tilting the head to the other side. By this procedure, equilibrium and a new order are obtained, which is confirmed by the fact that, under this condition, the patient feels best and shows normal behavior in all performances.

The difference of adjustment to the same, only quantitatively different defect, again shows that the *motive is to find a new order for the total organism.* That form of adjustment occurs which best guarantees this order under the given condition. We have, as in hemianopsia and hemiamblyopia, here, too, two different, yet *opposite* ways of procedure motivated by *the same trend,* on the one hand yielding to the defect, on the other hand *transformation of the whole function* of the concerned apparatus. Both ways do not represent adjustment of equal value for the total organism. Yielding is more natural, more automatical, demands less voluntary activity, and therefore insures more security. In the second case, the *normal form of functioning is changed.* It is more voluntary, leads more readily to fluctuation of function, includes less security, and admits greater possibilities for catastrophic reactions. But it is the only way to guarantee the order

of the whole organism *under the given condition.* Therefore, it is chosen, but only if the other way is impossible. Again, we see as a determining factor the tendency to achieve the optimal performance of the total organism.

It is certainly of general interest that the *same motive* can bring about *different, yet opposite, effects in behavior*—a phenomenon which we meet with all motivating factors. A strong need can be fulfilled by yielding or opposition, and that procedure is selected which best guarantees the possibility of self-realization of the *total* organism.

We have considered, till now, the way of adjustment from the viewpoint of the condition in a special part of the organism (a defect in a special performance field). However, the condition of the rest of the organism and the demands which arise from the outerworld have to be taken into consideration as well if we want to understand the behavior of the patient. Adjustment to a special defect is totally different if the special capacity could no longer be used by the organism because it has other defects which would make this impossible. For example, a patient with visual agnosia, *i.e.*, defect of recognition of seen objects, will try to improve his defect in such recognition by building up non-visual performances as substitutes. But he will do it *only if he can use them.* A patient who cannot use them because he is paralyzed at the same time and, thus, hampered in activity in general, will not build such substitutes at all or only to a smaller degree.

A corresponding procedure takes place if the demands coming from the outerworld differ in degree. If they are too great in respect to the patient's capacities, he gives in and does not adjust himself to the highest possible degree, apparently because it would be in vain and any attempt would produce catastrophe. He satisfies himself with a lower form of adjustment and, if he is not allowed to do that, he breaks down. If the demands are too small and the patient can do justice to them without changes of behavior, these do not occur. It again becomes evident that the motive of the way of adjustment is determined by the trend to come into a state which makes possible the best way of self-realization under the condition of the irreparable defect.

To summarize: *What can we gain from the experiences with patients with brain damage for our knowledge concerning the forces which determine motivation?* We saw that adjustment is determined by the significance which a special activity has for the organism as a

whole, and that the motivational force of this activity—yielding or transformation of function—depends upon this significance.

This is valid for adjustment to an irreparable defect as well as for the effect of normal needs. Any explanation is doomed to failure which attempts to reduce human motivation to a number of *isolable factors,* capacities, drives, etc., to *separated* forces which interact only secondarily with each other. Our analysis has shown that such constant and independent forces may determine behavior *under pathological and under unnatural, eventually emergency conditions.* They are due to the influence of isolation on the behavior which is characteristic for all these conditions. We have no right to infer, from these phenomena, the existence of such single forces in the normal organism.

Pathology teaches us that we have to be cautious with all such inferences. Thus, for instance, we have no right to assume, from these experiences, that the clue for motivation normally is tension-release. Such an assumption neglects the factor of pathology, of isolation in general, in modifying behavior: it is the effect of the fallacy of isolation.

Our main result was that the basic trend of the organism is the trend *to realize its capacities,* its *personality* as much as possible, that it is the trend for *self-realization.* Forces which may gain influence, as special needs, can be evaluated in their motivational effect only if they are considered from this point of view, from *their significance for self-realization of this or that organism*—normal and pathological under this or that condition.

Here, we have a new starting point and task for research. Our approach traces the whole problem of motivation back to the problem of the organization of the organism, its capacities and potentialities, *i.e.,* its *nature.* We are confronted, indeed, with a difficult scientific problem of methodology, namely, how to gain knowledge about this nature of the organism from phenomena which we have to obtain by an analytic, isolating procedure of investigation. Especially, the question has to be answered of how to differentiate between the phenomena that are more or less essential for the organism and such that are due to the artificial isolation. Certainly, I cannot enter into the discussion of this basic problem of psychology and anthropology here. I again wish to refer, in this respect, to my book, *The Organism.* There, I have discussed the general methodological problem involved and tried to find rules for this differentiation by pointing to the *material*

gathered under the concept of *preferred behavior*. This material seems to hold promise to make our task possible, at least in so far that we learn some steps of our way to the goal. The problem of motivation will not come on a more rational basis until the functional structure of the organism is better understood. I think that, in this respect, pathology can contribute very much, indeed, only if the phenomenon of pathology itself is taken into correct consideration.

I am fully aware that my dealing with the problem of motivation was incomplete, which is due partially to the complexity of the problem which could scarcely be disentangled sufficiently in one lecture. I was able to treat the problem only in a somewhat sketchy way. I could not do much more than to point to some material—by the way, easily to be multiplied—which may be useful in further discussion, and give some hints as to procedure in the attempt to find a more factual and reasonable basis for a theory of motivation. What I regret particularly is that I had no time to expose the implications of my interpretation of the facts as regards therapy, in patients with organic diseases as well as with neuroses. My point of view grew from the attempt to help patients. The problem of motivation is closely related to therapy. A theory of motivation should never forget that we are not primarily interested in this problem for the sake of knowledge, but for the sake of helping, guiding, of trying to change human behavior for the better. Therapy, on the other hand, cannot do anything more sensible than to observe the motivational tendencies operative in nature in the attempt of adjustment to defects, and then to try to follow these tendencies. There could be, in turn, no better proof for the soundness of this organismic approach to motivation than its usefulness for the purposes of therapy.

SECTION OF ANTHROPOLOGY

MARCH 24, 1947

DOCTOR JULIAN H. STEWARD, Department of Anthropology, Columbia University, New York, N. Y.: *American Culture History in the Light of South America.*

The data of the *Handbook of South American Indians* suggest a four-fold classification of native South American cultures: (1) the Marginal, or hunting-and-gathering tribes; (2) the Tropical Forest peoples; (3) the Circum-Caribbean tribes; and (4) the Central Andean civilizations.

The Marginal tribes resemble the non-farming tribes of North America in their lack of certain advanced technologies, such as farming, loom weaving, woven baskets, dugout canoes, building arts, and metallurgy, and in the presence of innumerable items found mainly outside the area of farming, such as twined or coiled baskets, bark canoes, scratching sticks, drinking tubes, hockey and other games, etc. These may be survivals of a pre-agricultural, inter-American culture, but Marginal sociopolitical groups show evidence of local development, with strong environmental conditioning.

A basic civilization built on agriculture became established in the highlands, from Bolivia to Mexico, and in Yucatán. It had intensive farming, developed weaving, ceramics, metallurgy, and building arts, a class-structured society, incipient states, and a priest-temple-idol cult. These generalized features are an abstraction of a culture which had distinctive local forms but which, in its inter-American aspects, may be called the Formative Period culture.

From the Formative Period culture developed the distinctive Andean patterns, noted for their technological attainments and for their political developments.

A Formative Period type culture spread, with certain distinctive South American features, to the Maya frontier in Central America, beyond which it had Mexican characteristics, and across northern South America to the Antillean Arawak. Its principle features were: matrilineal decent, classes based particularly on priestly and warrior groups, a priest-temple-idol cult, and such rain forest adaptations, shared also with the Tropical Forest peoples, as cultivation of fruits

and root crops, dugout canoes, pole-and-thatch houses, hammocks, bark cloth, and blow guns. The general pattern and certain specific elements of the Circum-Caribbean culture are also found in the southeastern United States, though the latter area is likewise linked to Mexico in some features.

It is postulated that the Tropical Forest tribes of Venezuela and the Guianas borrowed farming, pole-and-thatch houses, dugout canoes, pottery, and loom weaving from the Circum-Caribbean peoples, but they did not borrow the class-structured society or the priest-temple-idol cult. This material culture spread up the Amazon, but faded at its headwaters, leaving the tribes in a Marginal position culturally. These tribes are distributed in a great "U" around the Amazon Basin, and they extend to eastern Brazil and south through Mato Grosso, the Gran Chaco, and Pampas to the Chilean archipelago. The Tropical Forest technology was also spread, principally by Tupian tribes, down the coast of Brazil in the rain forest areas, and across Paraguay even to the Andes.

SECTION OF PHYSICS AND CHEMISTRY

MARCH 25, 1947

MR. J. J. BIKERMAN, Merck and Company, Inc., Rahway, N. J.: *Tackiness and Adhesion.* (This address was illustrated by lantern slides.)

(This paper will be published in the May issue of TRANSACTIONS.)

MR. ALLEN S. KENYON, Department of Chemistry, Columbia University, New York, N. Y.: *Higher Order Tyndall Spectra in Monodispersed Sulfur Sols.** (This lecture was illustrated by lantern slides and a demonstration.)

When light is passed through a relatively monodispersed colloid, in which the radius of the particles is roughly comparable to the wavelength of light and the index of refraction of the medium and dispersed phase differ appreciably, beautiful optical effects will be observed. These optical effects can appropriately be designated, "Higher Order Tyndall Spectra."

If white incident light is used, red and green bands will appear at various angles. The number of distinct bands of one wavelength that are observed in 180° will be set equal to the number of orders. This number does not necessarily correspond to any theoretical basis. The blue Tyndall spectra in the Rayleigh region ($r \ll 1/10$ the wavelength of light) will be assigned the order zero.

The sulfur sol system has been used for a quantitative study of these optical effects because it is ideally suited, since sulfur particles are spherical and are colorless to visible light. Sulfur sols can also be prepared relatively monodispersed by the action of acid on sodium thiosulfate, provided that the concentration range is .0005 to .0015 molar with respect to the thiosulfate, and if the acid does not exceed .003 molar.

The formation of sulfur particles from the acid-thiosulfate can be divided into three phases, namely: (a) Homogeneous, (b) Particle Transition, and (c) Heterogeneous. The homogeneous reaction begins immediately upon mixing the acid and thiosulfate with the formation of molecularly dispersed sulfur and proceeds until a definite degree of supersaturation is reached. At this point, sulfur particles begin to form, as evidenced by the appearance of the blue Tyndall beam. After the transition, the particles continue to grow. These three phases have been followed by means of transmittance at a wavelength where only the increase in sulfur would change the optical density of the system. Regardless of the initial concentration of thiosulfate and acid used, the optical density at the point of transition remains constant. This means that reaction continues to be homo-

* This address was delivered at the meeting of the Section of Physics and Chemistry on February 28, 1947.

geneous until a definite degree of supersaturation is reached. It was found that the concentration of molecularly dispersed sulfur present at the time of transition was 5×10^{-6} gram atoms per liter. The formation of sulfur particles is an agreement with Von Weimarn's conclusions on "corresponding crystallization conditions." The kinetics of this reaction are being thoroughly investigated by Miss Ethel Zaiser under Prof. LaMer's direction.

The sulfur sols produced are more monodispersed than other sulfur sols that have been studied in the past. These sols have been examined under the ultramicroscope and the electron microscope. However, to date, no distribution values are available. Qualitatively, these sols are relatively monodispersed.

The angles at which orders appear are functions of the composition of the incident light, the particle size, and the relative refractive index of the particle to that of the medium. When the sulfur particles reach a size to produce orders, that is, $\alpha = 2$ where $\alpha = \frac{2\pi r}{\lambda'}$, r being the radius of the particle and λ' the wavelength of light in the medium, the order begins to form in the forward direction. As the particles grow, the number of orders increases from one to nine. This is the maximum number of orders that have been clearly distinguished.

The angular positions of orders are calculated theoretically as a function of size for a particular relative index of refraction. The calculations were based upon the Mie theory and were made for particle size studies on aerosols during the past war. In order to measure the particle size, it is necessary to measure the actual angular position of orders of a particular wavelength and read the size directly from the theoretical plot. The theoretical calculations were checked by an independent method using Stokes' Law.

The transmitted light can also be used as a means of determining the particle size. Moreover, this enables the number of particles per cc. to be measured. The total decrease in transmittance is due to scattering and any energy lost by molecular absorption. The optical density is expressed by

$$\log Io/I = K_s \pi r^2 nl/2.3, \text{ or} \qquad (1)$$

$$\log Io/I = K_e \pi r^2 nl/2.3 \qquad (2)$$

where Io/I is the ratio of the incident to transmitted light, K_s the scattering area coefficient, K_e the extinction area coefficient, n the number of particles per cc. and r the radius of the particles. EQUATION 1

applies to wavelengths where there is scattering only, and EQUATION 2 to those wavelengths where absorption is also present. K_s and K_e have units of area and are equal to the optical area effective in scattering light.

A plot of the K_s or K_e values against α for a constant relative refractive index passes through a minimum. When the transmittance of a sol is measured as a function of wavelength, the density will pass through a minimum which also corresponds to the theoretical minimum. The radius of the particles is then calculated from the relation $\alpha(\text{min.}) = \frac{2\pi r}{\lambda'(\text{min.})}$. The number of particles is calculated by using EQUATIONS 1 or 2, depending on whether or not absorption is present.

If the particles absorb, then the relative index of refraction becomes complex and is equal to $m = m'(1\text{-}ik)$, where m is the complex index, m' the ordinary index, and k the absorption index. This introduces a complication in the transmittance method, and the case is being thoroughly studied in the ultraviolet, where sulfur particles absorb. The details of this investigation will be reported elsewhere.

It has been shown how two different optical methods can be used to determine size when the particle size is comparable to the wavelength of light. Also, the transmittance method gives a simple means of determining particle number. These methods are only applicable for a limited number of systems, because of the very limited theoretical calculations available at present. As soon as the calculations are extended, these methods will be adaptable to many systems.

I wish to acknowledge due credit to Prof. V. K. LaMer and his other research students who made this presentation possible through their work.

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GENERAL CONFERENCE

March 21 and 22, 1947

Conference on *"The Adrenal Cortex."*

The New York Academy of Sciences and The New York Academy of Medicine jointly held a Conference on "The Adrenal Cortex." Doctor Robert Gaunt, Syracuse University, Syracuse, N. Y., was the Conference Chairman in charge of the meeting.

The program consisted of the following papers:

Friday, March 21

Morning Session. "Introductory Remarks," by the Conference Chairman.

"The Pituitary-Adrenal System," by George Sayers and Marion A. Sayers, Department of Pharmacology, University of Utah School of Medicine, Salt Lake City, Utah.

"The Chemistry and Partial Synthesis of Adrenal Steroids," by Edward C. Kendall, Division of Biochemistry, Mayo Foundation, Rochester, Minnesota.

"The Bioassay of Adrenal Cortical Hormones," by Ralph I. Dorfman, Department of Medicine and Biochemistry, Western Reserve University, School of Medicine and Lakeside Hospital, Cleveland, Ohio.

Afternoon Session. "Some Studies on the Role of the Adrenal Cortex in Organic Metabolism," by Dwight J. Ingle, Research Laboratories, The Upjohn Company, Kalamazoo, Michigan.

"The Cytology and Cytochemistry of the Adrenal Cortex," by Roy O. Greep and Helen Wendler Deane, Harvard School of Dental Medicine, and Department of Anatomy, Harvard Medical School, Boston, Massachusetts.

"The Adrenal Cortex and Its Tumors," by George W. Woolley, Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine.

Saturday, March 22, 1947

Morning Session. "Urinary Excretion of Adrenal Cortical Steroids," by Eleanor H. Venning and J. S. L. Browne, Royal Victoria Hospital, Montreal, Canada.

"Adrenal Cortex Function in Stress," by Gregory Pincus, Worcester Foundation for Experimental Biology, Shrewsbury, Massachusetts.

"The Diseases of Adaptation," by Hans Selye, University of Montreal, Montreal, Canada.

Afternoon Session. "Clinical Studies in Addison's Disease," by George W. Thorn, Peter H. Forsham, F. T. Garnet Prunty, and A. Gorman Hills, Department of Medicine, Harvard Medical School, and the Medical Clinic, Peter Bent Brigham Hospital, Boston, Massachusetts.

"Cushing's Syndrome—A Disease of the Adrenal Cortices?" by E. J. Kepler, Mayo Clinic, Rochester, Minnesota.

NEW MEMBERS

Elected March 27, 1947

LIFE MEMBERSHIP

Jarcho, Saul, M.D., Pathology, Parasitology. Assistant to Director of Clinical Research, Mount Sinai Hospital, New York, N. Y.

ACTIVE MEMBERSHIP

Abramson, Samuel, V.M.D., Experimental Pathology (Tuberculosis). Assistant Scientist (Veterinarian), Tuberculosis Control Division, U. S. Public Health Service; at Henry Phipps Institute, Philadelphia, Pa.

Anshen, Ruth Nanda, Ph.D., Psychology. Editor, Science of Culture Series, New York, N. Y.

Baker, Bernard R., Ph.D., Organic Chemistry. Chemist, Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y.

Ballinger, Joseph, M.D., Medicine. New York, N. Y.

Bates, Robert W., Ph.D., Endocrinology. Head, Endocrine Products Department, E. R. Squibb & Sons, New Brunswick, N. J.

Behnke, A. R., M.D., Application of Physiologic Principles to Problems in Military Medicine. Research Executive, Naval Medical Research Institute, National Naval Medical Center, Bethesda, Md.

Blain, James H., Jr., M.D., Biology. Attending Surgeon, Alexander Blain Hospital, Detroit, Mich.

Bowman, Robert L., M.D., Physiology. Research Fellow, New York University Research Service, Goldwater Memorial Hospital, Ward's Island, N. Y.

Buschke, William H., M.D., Biology, Biophysics, Biochemistry. Director of Ophthalmic Research Laboratory, Manhattan Eye, Ear and Throat Hospital, New York, N. Y.

Cantarow, Abraham, M.D., Biochemistry, Physiology. Professor of Biochemistry, Jefferson Medical College, Philadelphia, Pa.

Cargill, Walter Hurt, M.D., Renal Physiology. Fellow in Medicine, Department of Medicine, Duke University School of Medicine, Durham, N. C.

Cohn, Theodore D., M.D., Internal Medicine, Physiology, Biochemistry. Coney Island Hospital, Brooklyn, N. Y.

Coonfield, Benjamin Randolph, Ph.D., Zoology, Biology, Physiology, Neurology. Associate Professor of Biology, Brooklyn College, Brooklyn, N. Y.

Costello, Donald Paul, Ph.D., Experimental Embryology, Cytology, General Physiology. Professor of Zoology, University of North Carolina, Chapel Hill, N. C.; Instructor in Charge of Embryology, Marine Biological Laboratory, Woods Hole, Mass.

Cotlove, Elaine Wolf, M.D. Research Fellow in Cardiology, Cornell University Medical College, New York, N. Y.

Cotlove, Ernest, M.D., Internal Medicine, Hematology, Cardiovascular Physiology. Fellow in Medicine, Third (New York University) Medical Division, Goldwater Memorial Hospital, Welfare Island, N. Y.

Craver, Lloyd F., M.D., Internal Medicine as Related to Cancer. Assistant Professor of Clinical Medicine, Cornell University Medical College; Attending Physician, Memorial Hospital for Treatment of Cancer, New York, N. Y.

Diamond, Grant S., Ceramics. President, Electro Refractories and Alloys Corporation, Buffalo, N. Y.

Di Lorenzo, Joseph J., M.S., Bacteriology, Immunology. Bacteriologist, Food and Drug Administration, Penicillin Control and Immunology, Department of Agriculture, Washington, D. C.

Di Maio, Dominick J., M.D., Biochemistry, Pathology. Assistant Pathologist, Israel Zion Hospital, Brooklyn, N. Y.

Dreyfus, Camille, M.D., Hematology, Internal Medicine. Clinical and Research Assistant, Mount Sinai Hospital, New York, N. Y.

Durfee, Grace R., B.S., Biology. Director of Biological Laboratory, Applied Research Laboratories, Dayton, N. J.

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